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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,721	MCCART ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15,17,18,25 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15,17,18,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☒ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Non-Final Office Action is a reply to the "AMENDMENT AND RESPONSE TO OFFICE ACTION" of 25 September 2003 (hereinafter, 25 September Paper) filed in response to the Non-final Office Action mailed 20 May 2003 (hereinafter, 20 May Office Action). Claims 19-24 and 26 were withdrawn from consideration and claims 1-18 and 25 were considered in the 20 May Office Action. Claims 14, 16, 19-24 and 26 were canceled, claims 1-13, 15, 17, 18 and 25 were amended and claim 27 was added in the 25 September Paper. Claims 1-13, 15, 17, 18, 25 and 27 are pending and under consideration.

Response to Amendment

Objection and rejection of claims 14 and 16 is rendered moot by cancellation of the claims.

Claim Rejections - 35 USC § 112

Rejection of claims 17 and 18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn.

Claim Rejections - 35 USC § 102 and 103

Rejection of claims 1, 2, 5, 6-12, 15 and 25 under 35 U.S.C. 102(b) as being anticipated by Bodemer *et al.* (1991) EP 0 443 335 as evidenced by Kaplan, C. (1989) *Arch. Virol.* 106:127-139 and Buller *et al.* (1988) *J. Virol.* 62:866-874, rejection of claims 1-9, 12, 15 and 25 under 35 U.S.C. 102(b) as being anticipated by Paoletti *et al.* (1992) WO 92/15672, rejection of claims 1,

2, 5, 6-12, 13, 15 and 25 under 35 U.S.C. 103(a) as being unpatentable over Bodemer *et al.* as evidenced by Kaplan, C. and Buller *et al.* and further in view of any one of Lee *et al.* (U.S. Patent No. 5,851,991), Kamb (U.S. Patent No. 5,739,027), Herlyn *et al.* (U.S. Patent No. 5,622,835), Rotter *et al.* (WO 94/10575) or Spitsberg *et al.* (WO 98/08394), and rejection of claims 1, 2, 5, 6-12, 15 and 25 under 35 U.S.C. 103(a) as being unpatentable over Bodemer *et al.* (*supra*) as evidenced by Kaplan, C. (*supra*) and Buller *et al.* (*supra*) and further in view of any one of JP 55026477; Sawamura *et al.* (U.S. Patent No. 5,962,260); Cheng *et al.* EP 0 585 960; Boehmert *et al.* (DE 3411472); Rasmussen *et al.* (U.S. Patent No. 5,236,838); Kataoka *et al.* (JP 020655779); or Cheng *et al.* (U.S. Patent No. 5,981,714) is withdrawn. Although the art contemplates a vaccinia virus vector comprising a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype (see Bodemer *et al.* and Paoletti *et al.* and the discussion thereof in the previous Office Action), the cited art does not contemplate introducing the vector into a tumor cell wherein the tumor cell is present in a mammal. Further, although the art teaches that vaccinia virus vectors can be used to introduce genes into tumor cells *in vivo* (see, e.g., US Patent No. 6,093,700 and US Patent No. 5,744,133), that art does not contemplate using a vector comprising a negative vaccinia virus growth factor phenotype, and none of the art of record provides motivation to specifically substitute the vaccinia virus contemplated by Bodemer *et al.* and Paoletti *et al.* for the vector used in the methods of US Patent No. 6,093,700 and US Patent No. 5,744,133.

New Grounds

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13, 15, 17, 18, 25 and 27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to nonstatutory subject matter. The claims are directed to a tumor cell comprising a vaccinia virus expression vector, wherein the tumor cell is present in a mammal. The specification contemplates methods wherein the vaccinia virus vector of the claims is delivered to neoplastic cells of humans *in vivo* (see, e.g., paragraph [0069]). Thus, the claims clearly encompass a human cell *in situ,* and therefore a portion of a human being. In response to previous discussions (see the attached interview summary) Applicant argues that the tumor cell, being living subject matter is patentable subject matter. However, MPEP 2105 also states, "if the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter." As the claims are clearly directed to a portion of a human being which has not been isolated from the human, the claims read on the human being itself and are therefore nonstatutory subject matter. Applicant cites US Patent No. 5,869,040 as containing claims directed to a tumor cell; however, each application for a patent must be evaluated on its own merits and present Office Policy is to reject claims to cells of human beings *in situ* as nonstatutory.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 12, 13, 15, 17, 18 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims are directed to a tumor cell comprising a vaccinia virus expression vector, wherein said expression vector comprises a negative vaccinia virus growth factor phenotype. The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Federal Register, Vol. 66, No. 4, Column 1, page 1105). In the instant case, the vaccinia virus vector comprising a negative vaccinia growth factor phenotype is clearly a critical element of the invention and must be adequately described. The specification teaches, "[a] vaccinia virus with a negative VGF phenotype can be made in a manner similar to that described for the TK gene. For

example, one or both of the VGF genes can be inactivated..." (paragraph [0025]). Unlike the TK- phenotype, wherein the specification teaches, "it is necessary to disrupt the nucleic acid sequence of the TK gene in such a way that the TK gene no longer encodes an active and functional copy of the TK gene" (paragraph [0024]), the vector comprising a VGF- phenotype does not require disruption of the nucleic acid sequence encoding one or both of the VGF genes such that the genes are inactivated. Thus, the claims encompass a tumor cell comprising any vaccinia virus expression vector comprising a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype, including those wherein the vector comprises functional VGF genes. However, the specification is silent with regard to manipulations of vaccinia virus that would produce a vector having a VGF- phenotype other than disruption of the VGF genes such that the genes no longer encode an active and functional copy of the VGF gene. Thus, the skilled artisan would not be able to envision embodiments of the claimed invention beyond the scope of those wherein the VGF genes are disrupted.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of any vaccinia virus expression vector comprising a negative VGF phenotype. Therefore, only the described embodiments wherein the negative VGF phenotype results from deletion of one or more VGF genes, deletion of a portion of one or more VGF genes, deletion of the EGF-receptor binding site of VGF or an insertion in one or more VGF genes meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-6, 12, 13, 15, 17, 18 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a tumor cell comprising a vaccinia virus expression vector with a negative VGF phenotype, wherein the negative VGF phenotype results from deletion of one or more VGF genes, deletion of a portion of one or more VGF genes, deletion of the EGF-receptor binding site of VGF or an insertion in one or more VGF genes, does not reasonably provide enablement for the claimed invention wherein the negative VGF phenotype results from some modification of the vector other than those resulting in direct modification and inactivation of the VGF genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: As discussed above, the claims broadly encompass a tumor cell comprising a vaccinia virus expression vector, wherein the vector comprises a negative VGF phenotype resulting from any modification of the vector.

State of the prior art and level of predictability in the art: The art is silent with regard to how one might make a vaccinia virus vector having a negative VGF phenotype beyond direct inactivation of the VGF genes themselves. As the art provides no basis to predict what manipulations might produce a negative VGF phenotype other than modification of the VGF genes, the skilled artisan is fully dependent upon the teachings of the specification to set forth a process of making the invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the same.

Amount of direction provided by the inventor and existence of working examples: With regard to embodiments of vaccinia virus vectors comprising a negative VGF phenotype other than those comprising insertions or deletions in the VGF genes themselves, the specification provides no guidance beyond what was available in the art.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make the full scope of the claimed invention without having to engage in undue experimentation. The claims broadly encompass tumor cells comprising any vaccinia virus expression vector having a negative VGF phenotype, yet the teachings of the specification provide instruction that would enable the skilled artisan to make only those embodiments wherein the vector comprises inactivating insertions or deletions in the VGF genes. In order to make the invention beyond this scope, the skilled artisan would have to resort to blind trial and error experimentation to identify mutations outside of the VGF gene that result in a negative

VGF phenotype. Therefore, it would require undue experimentation to practice the invention commensurate with the full scope of the claims.

Response to Remarks Regarding Compliance with Utility Requirement

A review of the specification reveals several contemplated utilities for the tumor cell of the claims. In Example 9, the tumor cells express a HER2 protein which is used to identify the cells as a target for Herceptin. In Examples 10 and 11, the cells express proteins used for tumor imaging. In Example 13, the cells express proteins that induce a cellular immune response against the tumor and in Example 14, the cells express suicide genes which destroy the cells. Furthermore, the disclosure provides evidence that the tumor cells of the invention selectively replicate the vaccinia virus vector which also leads to the demise of the cancer cells.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DMS

DAVID GUZO
PRIMARY EXAMINER